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| EXAMINER | |
|---|---|
| KAUSHAL, SUMESH | |
| ART UNIT | PAPER NUMBER |
| 1633 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/924,011 | DEPHILLIPO ET AL. | |
| | Examiner | Art Unit | |
| | Sumesh Kaushal | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *14-17,20-27,30-33,63 and 65-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17,20-27,30-33,63 and 65-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's response filed on 11/16/07 and Dr. Ricciardi's declaration (11/16/07) has been acknowledged and fully considered.

*Claims 69-73 are newly filed.*
*Claims 14-17, 20-27, 30-33, 63, 65-73 are pending and are examined in this office action.*

*Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is* ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

### *Claim Rejections - 35 USC § 112*

Claims *14-17, 20-27, 30-33, 63 and 65-70 are* rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reason of record as set forth in the office action mailed on 07/16/07.

Claim 65 is indefinite because it is unclear what encompasses “calculating a susceptibility value for the condition by either summing the identified polymorphisms to yield a value for the human, or assigning a weighting factor to each polymorphism and then summing the weighting factors to yield a value for the human”. For example it is unclear what is the criterion used to yield polymorphism values and weighing factors especially in the context of a control. Furthermore it is unclear what are the metes and bounds of the control. The term "relative degree" in claim 65 is a relative term, which renders the claim indefinite. The term "relative degree" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 68 indefinite because it is unclear what encompasses "score correlating polymorphism homozygosity and a bone density associated disorder"

Claim 26 is indefinite because it is unclear what is the criterion used to calculate the susceptibility value for the gene encoding Vit.D Receptor and the gene encoding IL-6. For example it is unclear what encompasses "the product of a constant and correlation factor".

Claim 14 is indefinite because there is no nexus between the "occurrence of an individual disorder associated polymorphism" and the method of claim 65.

**Response to Argument** (indefiniteness)

The applicant argues that in view of Dr. Ricciardi's declaration the claims are sufficiently defined. The applicant argues that calculating susceptibility values for human is disclosed at least at para. 22 and 50-52, using values known to one of ordinary skill in the art. The applicant argues that the declaration asserts that the claims are sufficiently definite in demonstrating how to calculate the susceptibility value by summing, or by assigning a weighting factor and then summing, each polymorphism in each of the vitamin D receptor gene and the IL-6 gene, as claimed. Regarding the "relative degree of an undesirable bone density" the applicant argues that specification discloses a method of assessing the relative susceptibility of a human to an undesirable bone density condition and the susceptibility can be calculated relative to a hypothetical human or alternatively can be calculated relative to another human. Regarding the "score correlating polymorphism homozygosity and a bone density associated disorder" (claim 68) the applicant argues that the Declaration describes why such a correlating score is not unclear as the declaration provides an analysis of the weighting factor. Regarding the issue "the product of a constant and a correlation factor", (claim 26), the applicant argues that as described at least at ¶22, the weighting factor, which is summed to provide the susceptibility value, is calculated by multiplying the constant with the correlation factor for that polymorphism. Similarly the applicant's declaration asserts that invention as claimed is not indefinite because the invention could be practiced given the guidance and examples provided in the declaration (see Appendix A).

However this is found not persuasive. Although a claim should be interpreted in light of the specification disclosure, it is generally considered improper to read limitations contained in the specification into the claims. See In re Prater, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969) and In re Winkhaus, 527 F.2d 637, 188 USPQ 129 (CCPA 1975), In re Van Guens, 988 F.2d 1181, 26 PSPG2d 1057 (Ded. Cir. 1991), which discuss the premise that one cannot rely on the specification to impart limitations to the claim that are not recited in the claim. In the instant case even the details provided in the declaration are not fully supported by the specification as filed.

In addition if the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph would be appropriate. See Morton Int 'l, Inc. v. Cardinal Chem. Co., 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993). See MPEP 173.02. In instant case it is unclear how one would envision the invention as claimed to avoid infringement issues especially in context with "calculating a susceptibility value" as claimed. In addition the declaration discusses Skin SNPs (MSOD and GPX1), but falls short of providing any calculation to assess relative degree to which a human is susceptible to an undesirable bone density using vitamin D receptor and a human gene encoding interleukin-6 polymorphic forms.

***Claim Rejections - 35 USC § 112***

Claims *69-73 are* rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter). The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Regarding newly filed claims 69-73 the applicant fails to indicate where in the specification as filed there is support for newly filed limitation as claimed. A careful review by the examiner of the specification failed to identify any support for this new

limitation. Since no basis has been found to support the new claim limitation in the specification, the claims are rejected as incorporating new matter. As MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Claims *14-17, 20-27, 30-33, 63, 65-73* are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reason of record as set forth in the office action mailed on 07/16/07.

Claims *14-17, 20-27, 30-33, 63 and 65-73* are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reason of record as set forth in the office action mailed on 07/16/07.

**Response to arguments and Dr. Ricciardi's declaration** (*Written description and Enablement)*.

To support the lack of adequate disclosure and guidance encountered in the specification as filed (that would enable one ordinary skill in the art to practice the invention as claimed without undue amount of experimentation,) the applicant argues that in view of literature found a the time of filing and applicant's recent declaration, one ordinary skill in the art can determine what is required (material and methods) to practice the invention as claimed. The applicant argues that the specification at p.15 describes a bone density associated polymorphism in each of the human vitamin D receptor gene and the IL-6 gene. The applicant continues that in view of the current declaration, one of ordinary skill in the art can readily recognize first and second oligonucleotides based on this information. Additional bone density associated

polymorphisms in these two genes are known in the art, and thus one of ordinary skill in the art can determine first and second oligonucleotides based on this information.

However the applicant's arguments are found not persuasive. As stated earlier the scope of invention as claimed encompasses "*assessing a relative degree to which a human is susceptible to an undesirable bone density condition by identifying a polymorphic form identified as associated with any pathology in any gene-variant encoding a vitamin D receptor and any gene-variant encoding interleukin-6 present in the human's genome*" which requires the possession and enabled use of any and all polymorphic genetic sequences associated with a human gene encoding a vitamin D receptor and a human gene encoding interleukin-6 in context of any kind of undesirable bone density. The specification fails disclose any variants of gene encoding vitamin D receptor and interleukin-6 and association thereof with any kind of undesirable bone conditions *(i.e. bone formation, bone erosion and bone resorption etc.),* which would enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation. For example, the specification as filed even fails to disclose first and second oligonucleotides required for identifying any and all polymorphic forms of vitamin D receptor and Interleukin-6 wherein the polymorphic form is associated with any kind of undesirable bone density condition.

In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete structure. The specification fails to disclose representative number of species by structure and function encompassed by genus as claimed (i.e. any polymorphic form of vitamin D receptor and a human gene encoding interleukin-6 associated with any undesirable bone density condition). Claiming all divergent species that achieve a result as contemplated by the application without defining the representative number of species by structure and function is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. "The written description requirement has several policy objectives. The essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed." In re

Barker, 559 F.2d 588, 592 n.4, 194 USPQ 470, 473 n.4 (CCPA 1977). Another objective is to put the public in possession of what the applicant claims as the invention. See Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1566, 43USPQ2d 1398, 1404 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998)."

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. *Possession may be shown by an actual reduction to practice, showing that the invention as claimed is "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention* (see January 5, 2001 Fed.Reg., Vo.66, No. 4, pp. 1099-11).

In instant case the specification fails disclose the polymorphic form(s) of gene encoding vitamin D receptor and interleukin-6 associated with any undesirable bone density condition (*i.e. bone formation, bone erosion and bone resorption etc.),* which would enable one skilled in the art to practice the invention as claimed to without further undue amount of experimentation. Since the specification fails to disclose nucleotides required to practice the instant invention, defined by structure and function, it is not possible to envision the claimed composition. One cannot describe what one has not conceived. (See Fiddes v. Baird, 30 USP2d 1481 at 1483). According to these facts, one skill in the art would conclude that applicant was not in the possession of invention as claimed.

Regarding the enablement issues, even though candidate argues that the gene association studies are relatively easy to perform, the earlier office action clearly provides the evidence that the disadvantages include the possibility of false positive (or false negative) results due to confounding factors and population stratification.

The applicant fails to consider that the demonstration of an association between a candidate gene and BMD does not necessarily mean that the gene is causally

responsible for the effect observed. The state of the art at the time of filing clearly states that the associations can also occur as the result of linkage disequilibrium with a causal gene situated nearby on the same chromosome. (See Ralston J Clin Endocrinol Metab. 87(6):2460-6 2002, Zajikova et al Endocr Regul. 37(1):31-44, 2003). Thus the burdens shifts to applicant to establish that the one skilled in the art would able to practice the invention as claimed in view of limited amount of guidance provided in the specification without further undue amount of experimentation.

As stated above the scope of invention as claimed encompasses "*assessing a relative degree to which a human is susceptible to an undesirable bone density condition by identifying a polymorphic form identified as associated with any pathology in any gene-variant encoding a vitamin D receptor and any gene-variant encoding interleukin-6 present in the human's genome*", which requires the possession and enabled use of any and all polymorphic genetic sequences associated with a human genes encoding a vitamin D receptor and interleukin-6 associated with any undesirable bone density condition *(i.e. bone formation, bone erosion and bone resorption etc.).* At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970).

The applicant fails to consider that the state of the art, which clearly teaches that demonstration of an association between a candidate gene and BMD does not necessarily mean that the gene is causally responsible for the effect observed. The specification even fails to establish any bone density condition (i.e. osteophorosis or high bone mass) associated with all polymorphic gene associated with Vitamin D receptor and Interleukin-6 genes. Therefore identification of Vitamin D receptor and Interleukin-6 genotypes is considered germane to practice the invention as claimed.

The specification fails to provide any evidence that establishes the association of any undesirable bone density conditions associated with the occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D

receptor and a cytosine residue at position -174 of the interleukin-6 gene promoter. The disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). Considering the instant specification it is even unclear how bone density is affected by the presence of these SNPs. In addition, the specification fails to provide any evidence, which establishes that assessment of these SNPs in any combination (as claimed) would be a better predictor of assessing an undesirable bone density as compared to identification of a single SNP.

It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of skill. The specification fails to enable one skill in the art to practice the invention as claimed without further undue amount of experimentation.

In instant case assessing any undesirable bone density conditions by genetic analysis of Vitamin D receptor and IL-6 genes (as claimed) is not considered routine in the art and without sufficient evidence that the combination of SNPs encoding any variant of Vitamin D receptor and IL-6 genes (especially in context of any undesirable bone density condition) would be a better predictor of assessing an undesirable bone density, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400

(Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

## *Conclusion*

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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